REMARKS

This Reply is in response to the previous Office Action mailed on July 22, 2004. Reconsideration and allowance of the pending claims in view of the above amendments and the following remarks is respectfully requested.

Claim Objection:

The Applicants acknowledge, with thanks the withdrawal of the objection to claim 9.

Rejection under 35 USC §101:

At page 3 of the Office Action, the Examiner has maintained the rejection of claims 4, 8, 9, and 24-29 under 35 U.S.C.§101. In summary, the Examiner has stated that the claimed isolated nucleic acid molecules are not supported by either a specific and substantial credible asserted utility or a well-established utility and, consequently, the skilled artisan would not know what the protein does.

The Examiner again stated, without factual evidence to support his position, that he views the homology disclosed in the present specification to be too low for a skilled artisan to "know what the specific function of the claimed invention would be." The Applicants repeat their previous responses that the claimed isolated nucleic acid molecules, such as SEQ ID NOS:1 and 3, that encode a specified amino acid sequence, SEQ ID NO:2, and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 U.S.C.§101 and the first paragraph of 35 U.S.C.§112. These, as well as the accepted state of the art view that such molecules have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets, establishes the utility of the claimed invention.

Applicants have also provided further support to the functional claim of the present invention. The Hmmer search result shows that the protein of the present invention has a statistically significant domain of ATP synthase subunit C. Homology search results reveal that the present invention has 52% homology with a tomato vacuolar protontranslocating ATPase. Hence, the domain of the ATPase of the present invention is highly conserved even at the low

homology, in contrast to the Examiner's assertion. However, the Examiner dismissed the arguments based upon his assertions that the Hmmer results are "presented in the specification with no explanation as to their significance," and that it would be "impossible for one of ordinary skill in the art" to interpret the results because there is an "absence of a meaningful explanation of the Hmmer search results in the disclosure."

The Applicants traverse the Examiner's assertions on two points. First, in he Applicant's response filed May 20, 2004 on page 4, last paragraph, the Applicants were pointing out that contrary to the assertions of the examiner, that even at 52% homology with the tomato vacuolar protontranslocating peptide, the peptide is still identified as an ATPase. Therefore, with the much higher homologies (71%) between the peptide of the invention and the human vacuolar ATP synthase would establish the present invention as an ATPase synthase, absent evidence to the contrary provided by the Examiner. Second, one of ordinary skill in the art would be well aware of how to interpret the Hmmer results, as the Hmmer sequence analysis software is available at no charge from the Washington University in St. Louis School of Medicine. Additionally, all the documentation, analysis methods and explanations are similarly available through the same source, merely by typing in "Hmmer" through any popular search engine, such as Google®. Therefore, the assertions of the Examiner that one of skill in the art would not understand the Hmmer results is unfounded, as the program is well known in the art, and thus it is not necessary for the Applicants to include the information in the specification. Therefore, Applicants maintain that the Hummer search result shows that the protein of the present invention has a statistically significant domain of ATP synthase subunit C. Consequently, the evidence as a whole supports the instant polypeptide as a vacuolar ATP synthase.

The Examiner further stated, without presenting factual evidence that "it is highly likely that it [the claimed invention] has other functions that are distinct form those of known ATP synthase subunits C." [insert added by Applicants for clarification] The Applicants contend that the Examiner is holding the Applicant's invention to an unsupported standard of an alternative and unsupported function of the claimed polypeptide. The Applicants maintain that the instant polypeptide also shares significant sequence identity with other vacuolar ATP synthase subunits (page 5 of the Office action dated February 24, 2003) as indicated in Figure 1, Page 2 of 2 and that the Examiner has not provided any evidence or teaching supporting the assumption of alternative

activity that would contradict Applicants' assertion that the instant polypeptide is indeed a vacuolar ATP synthase subunit. The Examiner appears to be requiring the Applicants to completely reduce to practice the claimed invention and to disprove his unsupported contention that the claimed invention has a different function, a standard that is clearly not supported in the statute or by the courts. An applicant need not have actually reduced the invention to practice prior to filing. *In re Gould v. Quigg,* 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed.Cir. 1987) The Examiner also stated that the teachings of the specification regarding the K^+ depletion and NaCl deficiency conditions as potential targets "is not a specific and substantial asserted utility; rather it is a hypothesis to be tested." With this statement, the Examiner again appears to be requiring reduction to practice of the invention and to require the Applicants to include in the specification what is known in the art.

Applicants maintain that a skilled artisan would recognize the importance of a vacuolar ATP synthase, which is well known in the art, and how the specification teachings address a real world problem. The specification teaches that the differential regulation of H+-K+-ATPases (HKAs) takes place at the molecular level in acid-base and electrolyte disorders as discussed by the Applicants in the Reply filed May 20, 2004. The art supporting the Applicant's position was discussed as well: ATP synthases are known in the art and function in cellular and physiological processes (Martinez-Zaguilan et al., Am. J. Physiol. Cell Physiol. Vol. 265, pp. C1015-C1029, 1993) identify vacuolar ATP synthase in the plasma membrane of human tumor cells; Brown et al. (J. Exp. Biol. Vol. 203, pp. 137-145, 2000) report vacuolar ATP synthase involved in renal acidification; Chatterjee et al. (Proc. Natl. Acad. Sci. USA Vol. 89, pp 6257-6261, 1992) identify osteoclast vacuolar ATP synthase that function in bone resorption and have been identified in the disclosure as having tissue specific expression patterns, the disclosed utilities do not require or constitute carrying out further research to identify or reasonably confirm a real world utility. The instant polypeptide is a vacuolar ATP synthase and therefore the disclosed utility is substantial. Applicants have previously argued that the prior art teaches vacuolar ATP synthase involved in renal acidification, and the role of vacuolar ATP synthase in osteoclast bone resorption (see Brown et al and Chatterjee et al).

Applicants have also argued (Applicants' response dated August 15, 2003) that the CCPA in *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980), clearly accepted a showing of less than a

specific therapeutic use of a claimed chemical compound as satisfying the utility requirement. Summarizing, Applicants argued that similar to the *Nelson* case, the instant vacuolar ATP synthase of SEQ ID NO: 2 has useful value in the drug discovery process even though the molecule may not be associated with a specific treatment and/or diagnosis of a particular disease.

The Examiner was still not persuaded in the Action mailed July 22, 2004 and argues that the facts in *Nelson v. Bowler* are different from those of the instant case. The Examiner continues to assert that the pharmacological activity demonstrated by *Nelson* was sufficient to satisfy the utility requirement and that no pharmacological activity has been demonstrated in the instant case. The Examiner also stated that the Applicants' disclosure "fails to provide anything more than a general assertion of utility in the specification." The Applicants disagree, as the specification identified the instant polypeptide as a vacuolar ATP synthase subunit, which is not general, but rather is specific. The Applicants maintain that in the instant case, the practical utility or "real world utility" is provided by disclosure of SEQ ID NO: 2 as a vacuolar ATP synthase. Like *Nelson*, which states that "knowledge of the pharmacological activity of any compound is obviously beneficial to the public," the knowledge that the polypeptide of the instant invention is a vacuolar ATP synthase brings benefit to the public.

Applicants have previously argued (Applicants' first response was dated August 15, 2003) that the utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). Summarizing, the polypeptides and encoding nucleic acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc.

The Examiner further cited *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) that "[u]nless and until a process is refined and developed tot his point where specific benefit wxists in currently available form-there is insufficient justification for permitting an Applicant to engross what may prove to be a broad field." The Examiner continues that *Brenner v. Manson* precludes granting a non-specific process claim, so as not to create a monopoly of knowledge. The Applicants point out that the present claims are product claims and the reduction of a process to produce a disclosed sequence is well known in the art given the disclosure of the claimed

sequences. Therefore, the Applicants assert that the basis to reject the claims is not present in *Brenner v. Manson*.

The Examiner also maintained his statement on page 10 of the present Office Action, that the "specific utility must actually be contemplated by the inventor." The Applicants have disclosed in the specification and maintained in their arguments, a specific utility of the invention. The Applicants also request the Examiner to clarify the standard upon which he makes the assertion. The Applicants would like the opportunity to review the case law or rule from which he derives this apparently new standard. "Actual" contemplation of the utility by the inventors of an invention has been set forth by the courts while reviewing cases for infringement, which is different than a standard for patentability and is improper for the Examiner to hold an Applicant to a standard set forth in infringement cases. Without proper citation and review of the source of the standard that a "specific utility must actually be contemplated by the inventor," the Applicants cannot properly traverse the rejection and therefore assert that the rejection is improper and must be withdrawn.

Applicants continue to argue that the disclosure of the function of the transporter is sufficient. Summarizing, novel transporter/nucleic acids are commercially useful for developing therapeutics/diagnostics for these and other pathologies and that not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses.

Applicants continue to argue that by placing a new member of the transporter protein family into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further discovery. The Utility requirement cannot be used to contradict the reasons for the patent system, to encourage early disclosures of inventions so that others can benefit from, improve upon, and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new transporter proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

At page 11 of the Office Action, the Examiner maintained the rejection of the claims 4under 35 U.S.C. §112, 1st paragraph, without further explanation. The Examiner has stated that

since the claimed invention is not supported by either a specific and substantial credible asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicants respectfully traverse this rejection based on the following remarks.

Applicants maintain their previous arguments, as set forth above, that the instant invention is a vacuolar ATP synthase subunit. The claimed invention is supported by a specific and substantial credible asserted utility and therefore one skilled in the art would know clearly how to use the claimed invention.

In view of law and fact, the utility standard interpreted by the USPTO guidelines is too high. The disclosure of activity of the expressed polynucleotide is not required by any statute or case law interpreting the utility requirement of Section 101, and the enablement requirement of Section 112, first paragraph. The commercial value of a gene that encodes a previously unidentified member of the transporter protein family, members of which are well known in the art to be commercially valuable drug targets, should be sufficient to satisfy the utility requirement. Applicants also argue that the Examiner's apparent insistence upon providing evidence of the activity of the claimed invention is not supported by the applicable statutes or rule. The Applicants assert that the activity of the encoded sequence is not relevant to its use to develop inhibitors for the activity of the target protein in a disease state. Applicants also assert that activity of a target enzyme is not required for its use in an antibody-based microarray analysis, for example. As only one enabled embodiment is required by the statute, the apparent requirement of the Examiner for the Applicants to provide evidence of activity or to identify the activity of the claimed invention, is irrelevant.

Therefore, applicants respectfully request that the Examiner withdraw the rejection.

Conclusions

Claims 4, 8-9, and 24-29 are currently pending.

In view of the above remarks and amendments, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the objections and rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent should the Examiner believe a telephone interview would advance prosecution of the application.

Respectfully submitted,

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By: _____

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